CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 15-2009: A 25-Year-Old Man with Coma after Cardiac Arrest

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PRESENTATION OF CASE

Dr. Mathias Lichterfeld (Infectious Disease): A 25-year-old man was admitted to this hospital because of coma after cardiac arrest.

He had been well until 4 hours before admission, when he was seen to have had seizurelike movements and to have collapsed, without pulse or respirations. Emergency medical services was called and arrived approximately 7 minutes later. Examination disclosed ventricular fibrillation. Cardiopulmonary resuscitation, including the administration of epinephrine and atropine and electrical defibrillation followed by the administration of lidocaine, was performed; a junctional cardiac rhythm was established after 4 minutes. The patient remained hypotensive and unconscious. He was transported to this hospital. The trachea was intubated en route, and the lungs were ventilated by handheld bag.

There was no history of trauma, and the patient had no known illnesses. He had been born in South America and immigrated to the United States several years earlier; he was employed in construction and lived with relatives. On examination, he did not respond to voice, sternal rub, or nasal stimulation. The temperature was 36.1°C, the blood pressure 97/52 mm Hg (during the administration of norepinephrine by continuous infusion), the pulse 121 beats per minute, the respiratory rate 16 breaths per minute with assisted ventilation, and the oxygen saturation 96% while 100% inspired oxygen was delivered. The pupils were fixed and 8 mm in diameter, and blood was present in the nares. There were rare myoclonic jerks. There were no spontaneous respirations; oculocephalic, corneal, or gag reflexes; deep-tendon reflexes; or withdrawal in response to pressure on the deep nail beds or pinching of the extremities. He was incontinent of melanotic stool. Analysis of a urine specimen revealed cannabinoids and cocaine metabolites; other laboratory-test results are shown in Table 1. Urinalysis revealed a pH of 7.5, trace glucose, 3+ blood, 2+ protein, and trace urobilinogen, as well as 3 to 5 hyaline casts, more than 100 red cells, 50 to 100 white cells, many bacteria, and a moderate number of squamous cells per high-power field. Radiographs of the chest and abdomen and computed tomography (CT) of the head, cervical spine, chest, abdomen, and pelvis, after the administration of contrast material, showed no abnormalities. An electrocardiogram revealed sinus tachycardia at a rate of 133 beats per minute and was otherwise normal. Atropine

bicarbonate, crystalloid solution, norepinephrine, naloxone, lorazepam, and vecuronium were administered.

The patient was transferred to the coronary care unit, and external cooling was begun approximately 3 hours after cardiac arrest. Later that day, coffee-grounds material was aspirated from the oral gastric tube. Omeprazole was administered for gastric protection, and fluids and electrolytes were administered to maintain normal blood pressure and serum electrolyte levels. On the second hospital day, hypotension recurred that required pressor support, and cooling was stopped after 21 hours. Laboratory-test results are shown in Table 1. Specimens of blood and urine and nasal swabs were sent for culture and remained sterile, and no pathogens were identified by stool culture. Broad-spectrum antibiotics were administered intravenously, and supportive care was continued. The blood pressure continued to fluctuate, and the patient was intermittently febrile.

On the fifth hospital day, without sedation, the patient did not respond to any stimuli and the pupils did not constrict. Magnetic resonance imaging (MRI) of the brain after the administration of gadolinium revealed restricted diffusion, consistent with diffuse hypoxic–ischemic injury and right uncal and bilateral cerebellar tonsillar herniation. A radiograph of the abdomen showed possible thickening of the haustral folds of the transverse colon, suggestive of colitis. Mannitol was begun. CT of the head on the sixth and eighth hospital days revealed progressive loss of gray–white differentiation, with effacement of sulci, bilateral uncal herniation, and downward herniation of the contents of the posterior fossa. On the ninth day, a brain scan obtained after the administration of technetium-99m showed no appreciable uptake in the brain, and the patient met criteria for brain death.

The patient's family expressed a wish to donate his organs. The New England Organ Bank was consulted; a coordinator performed initial screening to confirm his suitability as a donor and obtained consent for organ donation. Echocardiography revealed no abnormalities and a normal ejection fraction, and cardiac catheterization revealed no coronary artery disease. Testing of the serum was positive for antibodies to cytomegalovirus (CMV) and Epstein–Barr virus (EBV) and negative for syphilis, human immunodeficiency virus (HIV) types 1 and 2, human T-lymphotropic virus (HTLV) types I and II, hepatitis C virus (HCV), and hepatitis B virus (HBV).

On the 11th hospital day, the patient was pronounced brain-dead and taken to the operating room for organ procurement. On initial inspection of the abdomen and pelvis, the cecum and ascending colon appeared inflamed and thickened. The heart, lungs, kidneys, liver, and pancreas were procured for transplantation.

A diagnostic procedure was performed.

DIFFERENTIAL DIAGNOSIS

Dr. Camille N. Kotton: This 25-year-old man with no known illnesses had a catastrophic event that resulted in brain death. His family generously agreed to donate his organs. With this patient, as with all potential organ donors, the transplantation team needs to make a rapid assessment of the suitability of his organs for donation. On initial evaluation, this patient appeared to be a good candidate for organ donation. The presence of a thickened colon, however, raised the question of whether there was a pathologic process such as an infection or a neoplasm that could be transferred to the recipient on transplantation. I was involved in this case and assisted the team in making this decision. The first step in the decision process starts with an evaluation by the organ bank, which was done in this case. Dr. Delmonico, will you discuss the role of the New England Organ Bank in assessing possible organ donors such as this one?

Dr. Francis L. Delmonico: The New England Organ Bank is 1 of 58 organ-procurement organizations that are members of the Organ Procurement and Transplantation Network that was established by Congress in 1984 and the United Network for Organ Sharing (UNOS).

In our region, the New England Organ Bank is notified of every imminent death in accordance with federal mandate. On notification, a donation coordinator makes an on-site evaluation as to whether the deceased person would be a suitable organ donor, as occurred in this case. The foundation of this assessment is to determine whether the organ is likely to function properly after transplantation and whether there are any infectious diseases or cancers that could be transmitted to the recipient through organ donation. The organ bank coordinates a standard evaluation to determine organ function (Table 2). Obtaining a detailed medical and social history is essential but

often difficult with a deceased donor. A thorough laboratory evaluation is also a critical part of the donor evaluation, especially in the assessment of infectious risk. Cultures of blood and urine are routinely obtained, and standard serologic testing is performed to detect potentially transmissible pathogens.

There have been numerous reports of donor-derived infections in solid-organ transplantation in the past few years, including rabies,[1,2] West Nile virus,[3] lymphocytic choriomeningitis virus,[4] Chagas' disease,[5,6] and HIV.[7] Prevention of donor-derived infections has been a main focus of the transplantation community. Several years ago, the Centers for Disease Control and Prevention (CDC) and UNOS, along with numerous other groups, were awarded federal funds to develop the Transplantation Transmission Sentinel Network, a network for detecting emerging infections among allograft donors and recipients. This network plans to improve information dissemination and allograft tracking by means of a secure Web-based electronic forum. The Diseases Transmission Advisory Committee of UNOS also monitors episodes of donor-derived infections and tumors.

Dr. Kotton: In this case, a coordinator from the New England Organ Bank performed a thorough assessment of the potential donor. In this previously healthy donor, exposures in his country of origin are the most significant risk factors for the transmission of infection to the organ recipient. All potential donors, however, undergo a standard

Table 1. Hematologic and Biochemical Laboratory Data.*

Variable	Reference Range, Adults†	On Admission
Hematocrit (%)	41.0–53.0 (men)	44.9
Hemoglobin (g/dl)	13.5–17.5 (men)	15.5
White cells (per mm^3)	4500–11,000	9100
Differential count (%)		
Neutrophils	40–70	85
Lymphocytes	22–44	11
Monocytes	4–11	3
Eosinophils	0–8	1
Platelets (per mm^3)	150,000–350,000	197,000
Mean corpuscular volume (μm^3)	80–100	83
Activated partial-thromboplastin time (sec)	22.1–34.0	84.5
Prothrombin time (sec)	10.3–13.2	19.8
International normalized ratio		1.9
Glucose (mg/dl)	70–110	236
Sodium (mmol/liter)	135–145	139
Potassium (mmol/liter)	3.4–4.8	4.0
Chloride (mmol/liter)	100–108	109
Carbon dioxide (mmol/liter)	23.0–31.9	21.8
Urea nitrogen (mg/dl)	8–25	18
Creatinine (mg/dl)	0.6–1.5	1.8
Lactate (mmol/liter)		4.1
Bilirubin (mg/dl)		
Total	0.0–1.0	0.3
Direct	0.0–0.4	0.1
Protein (g/dl)		
Albumin	3.3–5.0	4.1
Globulin	2.6–4.1	2.9

Table 1. (Continued.)

Variable	Reference Range, Adults†	On Admission
Phosphorus (mg/dl)	2.6–4.5	4.6
Magnesium (mmol/liter)	0.7–1.0	1.8
Calcium (mg/dl)	8.5–10.5	7.6
Alkaline phosphatase (U/liter)	45–115	184
Aspartate aminotransferase (U/liter)	10–40	220
Alanine aminotransferase (U/liter)	10–55	120
Lipase (U/dl)	1.3–6.0	6.0
Amylase (U/liter)	3–100	173
Creatine kinase (U/liter)	60–400 (men)	1,285
Creatine kinase isoenzymes (ng/ml)	0.0–6.9	19.7
Troponin T (ng/ml)	0.00–0.09	0.35

* To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for bilirubin to micromoles per liter, multiply by 17.1. To convert the values for phosphorus to millimoles per liter, multiply by 0.3229. To convert the values for magnesium to milliequivalents per liter, multiply by 2. To convert the values for calcium to millimoles per liter, multiply by 0.250.

† Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

evaluation, incorporating history, laboratory results, and intraoperative findings, for common infectious agents that may be easily transmitted from donor to recipient. In this case, laboratory evaluation included a battery of serologic tests for HIV, HBV, HCV, rapid plasma reagin, HTLV, CMV, EBV, and toxoplasma. Donor infection with HIV, HBV, or HCV is typically a "deal breaker" and would preclude donation except to previously infected recipients. Infection with other potential pathogens including EBV, CMV, and other herpesviruses do not preclude organ donation, but the information is used in assessing the risk of infection to the recipient and implementation of prophylactic or preemptive antiviral therapy. The CDC has defined exclusion criteria for organ donors that are based on behavior and history (Table 3) to reduce the potential for the transmission of HIV.[8]

Although our donor did not have any other worrisome infections that would preclude organ donation according to UNOS policy, certain severe and difficult-to-eradicate active infections (e.g., tuberculosis, Creutzfeldt–Jakob disease, and rabies) in a potential organ donor should preclude organ donation. Potential donors with controlled infections may be acceptable candidates.

This donor had no identifiable risk factors that would rule out donation. The donor was seropositive for CMV and EBV only; the recipient at our institution was seropositive for CMV and EBV, as well as for hepatitis C antibody and hepatitis B surface antibody; organ transplantation appeared to pose an acceptable risk to this donor–recipient pair.

Given the information available, our donor was considered medically suitable for donation, and the next step in the process was organ procurement. Dr. Elias, will you review the procurement procedure and your intraoperative findings?

Dr. Nahel Elias: We performed the procurement by means of a thoracoabdominal midline incision that allowed comprehensive exposure and exploration. The thoracic and abdominal great vessels were dissected. We cooled the organs in situ internally with preservation solution infused through the abdominal aorta and externally with sterile saline ice. Concurrently, the heart was arrested, and the cold ischemic time started. The blood was drained from the inferior vena cava, and the organs were sequentially recovered. We assessed the function of each organ on the basis of specific donor information (Table 2).

During the exploration, we noted an inflamed and thickened cecum and ascending colon. No other abdominal or thoracic abnormality was noted. I was concerned about the possible presence

Table 2. Organ-Specific Evaluation of a Potential Organ Donor.

Organ	Donor Characteristics and History	Laboratory and Investigational Data*	Intraoperative Assessment during Procurement	Special Considerations
Liver	Age Size of organ Substance abuse Hepatitis Obesity Hepatobiliary diseases	Liver-function tests	Contour Color Consistency	Biopsy (before or during procurement) to rule out fibrosis and macrovesicular steatosis (risk of primary nonfunction and transplant failure)
Kidney	Age Diabetes Hypertension Renal disease	Serum creatinine level Creatinine clearance rate Urinalysis (for proteinuria)	Size Parenchymal or vascular abnormalities	Biopsy to look for glomerulosclerosis, arterial atherosclerosis
Heart	Age Size of organ Cardiac or pulmonary disease	Chest radiograph Electrocardiogram Echocardiogram Coronary angiography	Volume status Cardiac injuries Strength of contractility Coronary calcifications	
Lung	Age Cardiac or pulmonary disease Size matched	Chest radiograph Oxygenation	Bronchoscopy Gross visual assessment	
Pancreas	Diabetes Severe alcoholism Morbid obesity	Serum amylase and lipase levels	Calcification Color Fat content	
Intestine	Age Intestinal diseases Hypotension and vasopressors (very sensitive) Long ischemia		Peristalsis Mesenteric arterial pulse	

* These data must be normal or trending to normal.

of colon cancer. Cancer transmission is minimized by excluding donors with active or recent cancer, except nonmelanoma skin cancer or in situ cervical cancer, since their transmission with transplantation is unprecedented.[9] Donors with cancers considered to be of low metastatic potential, such as certain tumors of the central nervous system or small renal-cell carcinomas, are variably used.[10] Highly metastatic cancers should be ruled out by history, physical examination, and thorough evaluation at the time of organ procurement.

After primary thoracic and abdominal dissection, the heart and lungs were procured, followed by the liver, pancreas, and kidneys. I then performed the diagnostic procedure — a full-thickness colon biopsy — and the specimen was sent for intraoperative examination of a frozen section. This was done after all organ recovery to avoid contamination with intraluminal colonic contents.

CLINICAL DIAGNOSIS

Cancer or infection of the colon in a brain-dead organ donor.

PATHOLOGICAL DISCUSSION

Dr. Richard L. Kradin: Examination of a full-thickness biopsy specimen of the cecum showed severe ulcerative ischemic necrosis of the bowel wall (Fig. 1A). The cecal mucosa contained numerous granulomas with refractile ova (approximately 150 μm in length) surrounded by epithelioid histiocytes, plasma cells, and eosinophils (Fig. 1B). Some of the ova showed well-developed lateral spines that stained with the Fite method (a weakly decolorized modification of the Ziehl–Neelsen acid-fast stain for mycobacteria) (Fig. 1C), whereas others had terminal spines (Fig. 1D). The appearances of the ova are consistent with schistosomal infection. Speciation of schistosomes is achieved by differences in morphology of the ova, with *Schistosoma mansoni* showing a well-developed lateral spine, whereas *S. haematobium* and *S. intercalatum* show well-developed terminal spines and *S. japonicum* shows a nonconspicuous terminal spine. In this case, the morphologic findings suggest a mixed infection, possibly with *S. haematobium* or *S. intercalatum*; within South America, only *S. mansoni* has been identified, in Brazil.

Table 3. Exclusion Criteria for Organ Donors, Based on Behavior and History.*

Men who have had sex with other men in the preceding 5 years
Persons who report nonmedical intravenous, intramuscular, or subcutaneous injection of drugs in the preceding 5 years
Persons with hemophilia or related clotting disorders who have received human-derived clotting-factor concentrates
Men and women who have engaged in sex in exchange for money or drugs in the preceding 5 years
Persons who have had sex in the preceding 12 months with any person described in the preceding four items or with a person known or suspected to have infection with the human immunodeficiency virus (HIV)
Persons who have been exposed in the preceding 12 months to known or suspected HIV-infected blood through percutaneous inoculation or through contact with an open wound, nonintact skin, or a mucous membrane
Inmates of correctional systems (the purpose of this exclusion is to address issues such as difficulties with informed consent and increased prevalence of HIV in this population)

* The data are from the Centers for Disease Control and Prevention.[8]

Dr. Kotton: The organ recipient at our institution was a 53-year-old woman with end-stage liver disease due to hepatitis C infection and end-stage renal disease due to fibrillary glomerulonephritis who had been receiving hemodialysis for 2 years. She was listed for both liver and kidney transplantation. The Model for End-Stage Liver Disease score was 30 (on a scale of 1 to 40, with a higher score indicating a greater severity of illness), predicting a 53% likelihood of death within 3 months.[11] When we learned that the donor had schistosomiasis involving the colon, we had to quickly assess the likelihood of transmission of this infection to the recipient and weigh this risk against the benefit of transplantation in a patient with a high likelihood of dying within the next 3 months.

In this case, our decision to accept this donor was complicated by the findings of active colitis presumed secondary to schistosomiasis. Schistosomiasis is an unusual finding in the evaluation of a prospective organ donor. Adult schistosomes do not replicate within the human host, because they need snails to serve as the intermediate host. Therefore, we were concerned about the transmission of nonreplicating adult worms, because they sometimes crawl into surgical sites and disrupt critical anastomoses. There have been several case reports that describe the successful use of organs from schistosoma-infected donors.[12-15]

In this donor, we also considered possible coexisting tropical infections, such as Chagas' disease (transmitted by *Trypanosoma cruzi*), *Strongyloides stercoralis*, *Paracoccidioides brasiliensis*, yellow fever, and leishmania, although some were ruled out by the length of time since he had left South America; the donor was later confirmed to be seronegative for *T. cruzi* and strongyloides. We considered numerous factors before deciding to proceed with the transplantation procedure, including the successes described in the literature, the availability of effective therapy, the fact that this was a potentially lifesaving two-organ transplantation, and that the initial liver biopsy showed no evidence of *S. mansoni*.

DISCUSSION OF MANAGEMENT

Dr. Elias: In this case, the heart, lungs, and liver were allocated by the New England Organ Bank. The primary liver recipient was a child; the transplantation surgeon accepted the left lateral segment and planned to split the liver. The right lobe of the liver and a kidney were offered to the recipient from this hospital, who was waiting for both. The other kidney was allocated separately. The transplantation surgeons in all cases were informed of the diagnosis of schistosomiasis in the donor and decided to accept the organs.

After the liver was split, we transplanted the right lobe into our recipient. During the same operation, she also received a kidney. The procedure was uneventful. On the first postoperative day, the recipient required an additional surgery for control of some intraabdominal bleeding. Her condition subsequently improved, and she was discharged on day 12. Her renal function was excellent 4 months later; she had liver dysfunction due to recurrence of HCV infection, which was treated and resulted in a partial response.

Dr. Eric S. Rosenberg (Pathology): Dr. Kotton, did you treat the recipient for schistosomiasis?

Dr. Kotton: Praziquantel was given to the recipient at 20 mg per kilogram of body weight (1700 mg) by mouth twice a day on postoperative

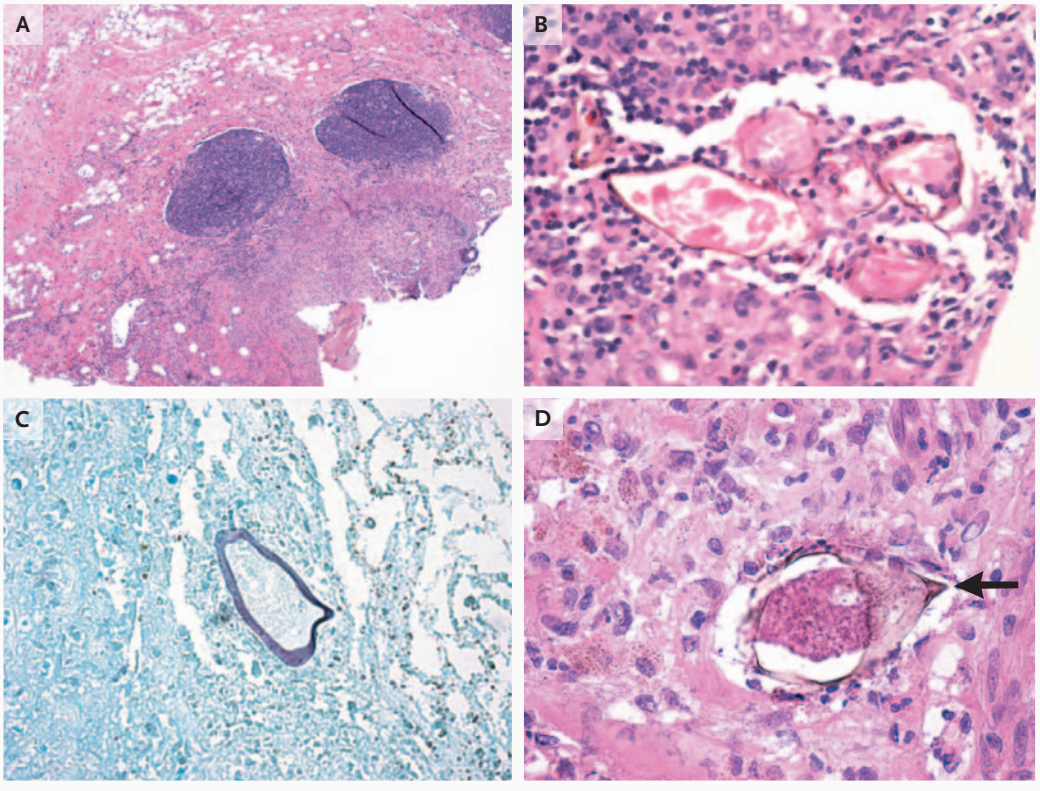

Figure 1. Colon-Biopsy Specimen.

An excisional biopsy of the cecum shows ischemic ulceration of the bowel wall (Panel A, hematoxylin and eosin). The cecal mucosa shows numerous circumoval granulomas with refractile ova (approximately 150 μm in length) surrounded by epithelioid histiocytes, plasma cells, and eosinophils (Panel B, hematoxylin and eosin). One ovum has lateral spines, which is morphologically consistent with the egg of *Schistosoma mansoni* (Panel C, Fite method). An ovum with a well-developed terminal spine (Panel D, arrow, hematoxylin and eosin) is consistent with the egg of *S. hematobium* or *S. intercalatum*.

days 1, 2, 3, 18, and 42 (to eradicate surviving schistosomes).

Dr. Nancy Lee Harris (Pathology): What happened to the other recipients?

Dr. Delmonico: They are fine; there has been no transmission of infection.

Dr. Nesli Basgoz (Infectious Disease): Should there be separate guidelines for the evaluation of donors who are foreign-born and from areas where these infections are endemic?

Dr. Kotton: There should be guidelines for additional screening when donors have had previous exposures in areas where the disease is endemic. As international travel increases, we may see more unusual and unexpected donor-derived infections.

Dr. Lloyd Axelrod (Medicine): Is the incidence of donor-derived infection increasing?

Dr. Kotton: We do not know whether the increase in reports of these infections reflects a true increase in cases, an increased recognition of the issue, or both. Certainly, infections will be more common, given the increase in world travel and in foreign-born organ donors in the United States.

A Physician: Do you routinely perform surgical evaluation of the intestine in potential organ donors? Were you planning on harvesting the intestine for bowel transplantation?

Dr. Elias: Examination of the bowel is part of the donor evaluation. However, a biopsy of the intestine would not normally be performed in a donor, such as ours, with a history of cardiac arrest

who is not considered as an intestinal donor because of prolonged bowel ischemia. The only reason for the biopsy in this case was because I palpated the colonic thickening. It is very unusual for a 25-year-old to have such an abnormality in the colon, and we were most concerned about detecting colon cancer. The thickened colon in this patient was diffuse, did not look like colon cancer, and was more consistent with colitis; there is, however, no harm in performing an additional biopsy.

A Physician: Were the other patients who received organs from this donor notified?

Dr. Elias: We informed all the other transplantation surgeons about our findings, and each transplantation surgeon made a decision regarding the risk versus the benefit of transplantation for their recipient. The risk has to be weighed against the seriousness of the disorders of the patient on the waiting list and the consequences of not receiving a transplant. For instance, we would not transplant this donor's pancreas, because it is not a lifesaving organ and there is some risk to the recipient.

Dr. Delmonico: When we detect the presence of transmissible infection in a potential donor, we do contact the donor's family if there is a potential health hazard to a family member.

ANATOMICAL DIAGNOSIS

Intestinal schistosomiasis in a brain-dead organ donor.

Dr. Delmonico reports receiving honoraria from Wyeth, Astellas, and Roche. No other potential conflict of interest relevant to this article was reported.

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